February 21, 2007

Edwin L. Mongan, III
Manager, Environmental Stewardship
E.I. du Pont de Nemours & Company
1007 Market Street
Dupont 6082
Wilmington, DE 19898

Dear Mr. Mongan:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the Fluoroethane Category, posted on the ChemRTK HPV Challenge Program Web site on April 27, 2005. I commend E.I. du Pont de Nemours & Company for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that DuPont advise the Agency, within 90 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact me at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Mark W. Townsend, Chief
HPV Chemicals Branch

Enclosure

cc: O. Hernandez
C. Augustyniak
J. Willis

EPA Comments on Chemical RTK HPV Challenge Submission:
Fluoroethane Category

Summary of EPA Comments

The sponsor, E.I du Pont de Nemours & Company, Inc., submitted a test plan and robust summaries to EPA for the Fluoroethane category, dated March 18, 2005. EPA posted the submission on the ChemRTK HPV Challenge Web site on April 27, 2005. The category consists of 1,1,2-trichloro-1,2,2-trifluoroethane (CAS No. 76-13-1), 1,1,1-trichloro-2,2,2-trifluoroethane (CAS No. 354-58-5), 1,2-dichloro-1,1,2,2-tetrafluoroethane (CAS No. 76-14-2), and 1,1-dichloro-1,2,2,2-tetrafluoroethane (CAS No. 374-07-2).

EPA has reviewed this submission and has reached the following conclusions:

1. Category Definition. The category is well defined.

2. Category Justification. The rationale and data presented in the test plan support the category.

3. Physicochemical Properties. The submitter needs to provide measured water solubility data for 1,1,1-trichloro-2,2,2-trifluoroethane (FC113a).

4. Environmental Fate. The data provided by the submitter for all SIDS endpoints are adequate for the purposes of the HPV Challenge Program.

5. Health Effects. The submitter needs to provide adequate data for the genetic toxicity (chromosomal aberrations) endpoint and address deficiencies in the robust summaries.

6. Ecological Effects. The submitter needs to provide adequate data for the algal toxicity endpoint and address deficiencies in the robust summaries.

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

EPA Comments on The Fluoroethane Category Challenge Submission

Category Definition

The category covers four perhalogenated ethanes containing fluorine and chlorine: 1,1,2-trichloro-1,2,2-trifluoroethane (FC-113), 1,1,1-trichloro-2,2,2-trifluoroethane (FC-113a), 1,2-dichloro-1,1,2,2-tetrafluoroethane (FC-114) and 1,1-dichloro-1,2,2,2-tetrafluoroethane (FC-114a).

Category Justification

The submitter justifies the grouping of the four fluorinated chloroethanes by their similarity in structures and resulting similarities in physicochemical, environmental fate, and toxicological properties. Overall, the rationale and data presented in the test plan support the category.

Physicochemical data: all four chemicals are volatile liquids or gases at room temperature. They also resist photodegradation by reactions with hydroxyl radicals, ozone, and nitrate radicals, but do undergo slow photolysis in the upper regions of the stratosphere. These fluorinated chloroethanes are not susceptible to hydrolysis under environmental conditions and resist biodegradation.

Health and ecological effects: the submitted data support the category approach by showing similar toxicological responses among the members.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data provided by the submitter for melting point, boiling point, vapor pressure, and partition coefficient are adequate for the purposes of the HPV Challenge Program.

Water Solubility. The submitter provided water solubility values of 170, 130, and 137 mg/L at 25 °C for FC-113, FC-114, and FC114a, respectively. While these values are similar, the submitter's estimated value of 20.9 mg/L for FC-113a is much lower. The submitter needs to locate a more credible value or provide measured water solubility data for FC-113a.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data provided for these endpoints are adequate for the purposes of the HPV Challenge Program.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The submitted data are adequate for the purposes of the HPV Challenge Program for all SIDS endpoints except genetic toxicity (chromosomal aberrations). The submitter needs to provide adequate data for the latter endpoint and address deficiencies in the robust summaries.

Genetic Toxicity (chromosomal aberrations). EPA does not consider data from a dominant lethal assay (of FC-113 in mice) adequate to address the chromosomal aberrations endpoint because the dominant lethal assay is designed to detect chromosomal damage only in germ cells (gonads), not in somatic cells. Therefore, the submitter needs to provide data from an *in vitro* chromosomal aberrations study, according to OECD TG 473, to adequately address this endpoint.

Ecological Effects (fish, invertebrates, and algae)

Fish. Adequate data for FC-113 and FC-114a are available for this endpoint for the purposes of the HPV Challenge Program.

Invertebrates. Adequate data are available for this endpoint for the purposes of the HPV Challenge Program. However, the submitter needs to address the deficiencies in the robust summaries.

Algae. Inadequate data are available for this endpoint; only ECOSAR-predicted algal toxicity values were provided. The submitter needs to either provide measured data on an analog supporting the ECOSAR-predicted algal toxicity values or test according to an OECD- and GLP-compliant method, with analytical monitoring of test concentrations, on both an FC-113 and an FC-114 series chemical.

Specific Comments on the Robust Summaries

Health Effects

Acute Toxicity. FC-113: The acute oral toxicity study summary needs the dose levels included. The acute inhalation toxicity study summary needs the LC_{50} units (ppm) converted to mg/m^3.

FC-114: The reliability statement for the acute oral toxicity study is inaccurate because the observation period (8 or 9 days) and the number of animals (1/dose group) used do not meet guideline requirements. The acute inhalation toxicity study summary needs LC_{50} units (ppm) converted to mg/m^3 and needs to indicate the period of observation.

FC-114a: The acute inhalation toxicity study summary needs LC_{50} units (ppm) converted to $mg/m^3$and needs to indicate the observation period.

Repeated-Dose Toxicity. Information missing from one or more study summaries included a list of hematological and clinical chemistry parameters evaluated, a list of tissues/organs histopathologically evaluated, and an explicit listing of NOAEL/LOAEL values.

Genetic Toxicity (gene mutations). The three gene mutation summaries lack information on the mean number of reverent colonies compared to controls. A study summary for FC-113 does not list the criteria for a positive response, statistical methods used, and whether the positive and negative controls responded appropriately. One summary (pp. 98-99) did not state whether a positive control was used.

Reproductive Toxicity. Information missing from the summary (FC-113) includes the mean measured test concentrations and an explicit statement of the NOAEL/LOAEL values determined. In the FC-114a dossier, the Reproductive Toxicity section includes a summary of an evaluation of male reproductive organs from the 2-week inhalation toxicity study. For the purposes of the HPV Challenge Program, the evaluation of reproductive organ toxicity is appropriate to address the endpoint only when it shows no effects in the 90-day repeated-dose toxicity study (in both sexes) and when a developmental toxicity study is available showing no effects. Therefore, the 2-week study summary needs to be deleted from this section.

Developmental Toxicity. The study summary (FC-113) lacks specification of the test guideline used and the explicit statement of NOAEL and LOAEL values for maternal and developmental toxicity.

Ecological Effects

Invertebrates. The summary of the study on FC-113 did not indicate the percentages of mortality/immobilization seen at each test concentration.

Followup Activity

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.